Claims

1. ~~A~~ Use of a composition comprising integrin alpha10-selected Mesenchymal Stem Cells (MSCs), for ~~use~~ the manufacture of a medicament for~~in~~ the treatment of a disease, disorder or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal.

2. The ~~composition for~~ use according to claim 1, wherein the disease of the respiratory system is a lower respiratory tract disease; or wherein the disease of the respiratory system is a respiratory disease principally affecting the lung interstitium; or wherein the disease of the respiratory system is a respiratory disease affecting the airways.

~~3. The composition for use according to claim 1, wherein the disease of the respiratory system is a respiratory disease principally affecting the lung interstitium.~~

~~4. The composition for use according to claim 1, wherein the disease of the respiratory system is a respiratory disease affecting the airways.~~

~~5.~~3. The ~~composition for~~ use according to any one of the preceding claims, wherein the disease of the respiratory system is a disease principally affecting the lung interstitium selected from the group consisting of acute respiratory distress syndrome (ARDS), pulmonary oedema , pulmonary eosinophilia, idiopathic interstitial pneumonitis, primary interstitial lung diseases specific to infancy or childhood, interstitial lung diseases associated with systemic diseases, pulmonary alveolar microlithiasis, lymphangioleiomyomatosis, and lipoid pneumonitis.

~~6.~~4. The ~~composition for~~ use according to any one of the preceding claims, wherein the disease of the respiratory system is acute respiratory distress syndrome (ARDS) and/or associated disorders.

~~7. The composition for use according to any one of the preceding claims, wherein the disease of the respiratory system is ARDS.~~

~~8.~~5. The ~~composition for~~ use according to any one of the preceding claims, wherein the disease of the respiratory system is cytokine release syndrome (CRS); or wherein the disease of the respiratory system is cytokine storm syndrome (CSS); or wherein the disease of the respiratory system is cytokine mediated ARDS; or wherein the disease of the respiratory system is ARDS/Respiratory distress syndrome of newborn, such as respiratory distress syndrome of newborn; or wherein the disease of the respiratory system is ARDS resulting from trauma; or wherein the disease of the respiratory system is ARDS caused by viral or bacterial infection; or wherein the disease of the respiratory system is ARDS resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) / COVID-19; and/or wherein the ARDS associated disease is multisystem inflammatory syndrome associated with COVID-19.

~~9. The composition for use according to any one of the preceding claims, wherein the disease of the respiratory system is cytokine storm syndrome (CSS).~~

~~10. The composition for use according to any one of the preceding claims, wherein the ARDS associated disease is multisystem inflammatory syndrome associated with COVID-19.~~

~~11. The composition for use according to any one of the preceding claims, wherein the disease of the respiratory system is cytokine mediated ARDS.~~

~~12. The composition for use according to any one of the preceding claims, wherein the disease of the respiratory system is ARDS/Respiratory distress syndrome of newborn.~~

~~13. The composition for use according to any one of the preceding claim, wherein the disease of the respiratory system is respiratory distress of newborn, such as respiratory distress syndrome of newborn.~~

~~14. The composition for use according to any one of the preceding claims, wherein the disease of the respiratory system is ARDS resulting from trauma.~~

~~15. The composition for use according to any one of the preceding claims, wherein the disease of the respiratory system is ARDS caused by viral or bacterial infection.~~

~~16. The composition for use according to any one of the preceding claims, wherein the disease of the respiratory system is ARDS resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) / COVID-19.~~

~~17. The composition for use according to any one of the preceding claims, wherein the disease of the respiratory system is ARDS resulting from any other cause.~~

~~18.~~6. The ~~composition for~~ use according to any one of the preceding claims, wherein at least 60% of the MSCs express integrin α10 subunit.

~~19. The composition for use according to any one of the preceding claims, wherein at least 50%, such as at least 55%, such as at least 60%, such as at least 65%, such as at least 70%, such as at least 75%, such as at least 80%, such as at least 85%, such as at least 90%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99%, such as at least 100% of the MSCs express integrin α10 subunit.~~

~~20.~~7. The ~~composition for~~ use according to any one of the preceding claims, wherein the MSCs are MHC class II, CD45, CD34, CD11b and/or CD19 negative, and/or wherein the MSCs express CD73, CD90 and/or CD105.

~~21. The composition for use according to any one of the preceding claims, wherein the MSCs express CD73, CD90 and/or CD105.~~

~~22.~~8. The ~~composition for~~ use according to any one of the preceding claims, wherein the MSCs are selected from the group consisting of a mesenchymal stem cells, mesenchymal progenitor cells, and mesenchymal stromal cells; or a

mixture thereof.

~~23.~~9. The ~~composition for~~ use according to any one of the preceding claims, wherein the MSCs are induced to express integrin α10 subunit.

~~24.~~10. The ~~composition for~~ use according to any one of the preceding claims, wherein the MSCs are cultured in a culture media comprising mammalian serum and FGF-2; or wherein the MSCs are cultured in a culture media comprising platelet lysate and/or platelet lysate components; or wherein the MSCs are cultured in a culture media comprising FGF-2 and platelet lysate and/or platelet lysate components; or wherein the MSCs are cultured in a culture media comprising mammalian serum and platelet lysate and/or platelet lysate components; or wherein the MSCs are cultured in a culture media comprising TGFβ; or wherein the MSCs are cultured in a culture media comprising FGF2; or wherein the MSCs are cultured in a serum-free culture media comprising platelet lysate and/or platelet lysate components; or wherein the MSCs are cultured in a serum-free culture media comprising growth factors; or wherein the MSCs are cultured in a serum-free culture media comprising the growth factors FGF2 and/or TGFβ.

~~25. The composition for use according to any one of the preceding claims, wherein the MSCs are cultured in a culture media comprising platelet lysate and/or platelet lysate components.~~

~~26. The composition for use according to any one of the preceding claims, wherein the MSCs are cultured in a culture media comprising FGF-2 and platelet lysate and/or platelet lysate components.~~

~~27. The composition for use according to any one of the preceding claims, wherein the MSCs are cultured in a culture media comprising mammalian serum and platelet lysate and/or platelet lysate components.~~

~~28. The composition for use according to any one of the preceding claims, wherein the MSCs are cultured in a culture media comprising TGFβ.~~

~~29. The composition for use according to any one of the preceding claims, wherein the MSCs are cultured in a culture media comprising FGF2.~~

~~30. The composition for use according to any one of the preceding claims, wherein the MSCs are cultured in a serum-free culture media comprising platelet lysate and/or platelet lysate components.~~

~~31. The composition for use according to any one of the preceding claims, wherein the MSCs are cultured in a serum-free culture media comprising growth factors.~~

~~32. The composition for use according to any one of the preceding claims, wherein the MSCs are cultured in a serum-free culture media comprising the growth factors FGF2 and/or TGFβ.~~

~~33.~~11. The ~~composition for~~ use according to any one of the preceding claims, wherein the MSCs are allogeneic or autologous.

~~34.~~12. The ~~composition for~~ use according to any one of the preceding claims, wherein the composition comprising the MSCs is formulated for administration~~administered~~ into the lung or airways.

~~35.~~13. The ~~composition for~~ use according to any one of the preceding claims, wherein the composition comprising the MSCs is formulated for administration ~~administered~~ via injection, and/or wherein the composition comprising the MSCs is formulated for administration parenterally.

~~36. The composition for use according to any one of the preceding claims, wherein the composition comprising the MSCs is administered parenterally.~~

~~37.~~14. The ~~composition for~~ use according to any one of the preceding claims, wherein the composition comprising the MSCs is formulated for administration ~~administered~~ via intravenous injection, intramuscular injection and/or intratracheal injection, or any combination thereof.

~~38.~~15. The ~~composition for~~ use according to any one of the preceding claims, wherein the composition comprising the MSCs is formulated for administration ~~administered~~ in a cell suspension with a pharmaceutically acceptable excipient.

~~39.~~16. The ~~composition for~~ use according to any one of the preceding claims, wherein the composition comprising the MSCs is formulated for administration ~~administered~~ during surgery to repair a damaged lung, and/or wherein the composition comprising the MSCs is formulated for administration in connection with lung transplantation.

~~40. The composition for use according to any one of the preceding claims, wherein the composition comprising the MSCs is administered in connection with lung transplantation.~~

~~41. The composition for use according to any one of the preceding claims, wherein the mammal is a human.~~

~~42. The composition for use according to any one of the preceding claims, wherein the MSCs and mammal are from the same species.~~

~~43. The composition for use according to any one of the preceding claims, wherein the MSCs and mammal are from different species.~~

~~44.~~17. The ~~composition for~~ use according to any one of the preceding claims, wherein the MSCs are derived from adipose tissue, bone marrow, synovial membrane, peripheral blood, cord blood, umbilical cord blood, Wharton's jelly, and/or amniotic fluid, such as MSCs derived from fetal, neonatal, juvenile or adult MSCs and/or progenitor cells; and/or MSCs not derived from embryonic cells or from an embryo.

~~45. The composition for use according to any one of the preceding claims, wherein the MSCs are derived from adipose tissue.~~

~~46. The composition for use according to any one of the preceding claims, wherein the MSCs are derived from bone marrow.~~

~~47. The composition for use according to any one of the preceding claims, wherein the MSCs are derived from fetal, neonatal, juvenile or adult MSCs and/or progenitor cells.~~

~~48. The composition for use according to any one of the preceding claims, wherein the MSCs are not derived from embryonic cells or from an embryo.~~

~~49.~~18. The ~~composition for~~ use according to any one of the preceding claims, wherein the MSCs are an in vitro cell culture.

~~50.~~19. The ~~composition for~~ use according to any one of the preceding claims, wherein the selection of MSCs has been conducted with an anti-integrin α10 antibody.

~~51. The composition for use according to any one of the preceding claims, further comprising an anti-inflammatory and/or immunomodulatory agent.~~

~~52. Use of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs), for the manufacture of a medicament for the treatment of a disease, disorder or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal.~~

~~53. A method of treatment of a disease, disorder or trauma of the respiratory system of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).~~

~~54. A method of treatment or promotion of a transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).~~

~~55. A method of preventing blood clotting in a mammal in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with~~

transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

56. A method of promoting hemodynamic stability in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

57. A method of reducing the need for inotropic support in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

58. A method of improving oxygenation capacity in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

59. A method of preventing tissue damage, for example structural tissue damage, in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

60. A method of reverting tissue damage, for example structural tissue damage, in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

61. The method according to any one of claims 59 to 60, wherein the tissue damage is lung tissue damage.

62. The method according to any one of claims 59 to 61, wherein the tissue damage is damage of the interstitial tissue, damage of the alveolar septa, damage of the airways, damage of the vasculature and/or damage of the nervous system.

63. A method of reducing neutrophil counts in connection with a disease, disorder, or trauma in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

64. A method of increasing lymphocyte counts in connection with a disease, disorder, or trauma in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

65. A method of decreasing proinflammatory cytokines in connection with a disease, disorder, or trauma in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).

66. The method according to claim 65, wherein the proinflammatory cytokines are selected from the group consisting of interleukin 12 (IL-12), IL-1β, IL-6 and IL-4, or any combination thereof.

~~67. The method according to any one of claims 65 to 66, wherein the proinflammatory cytokines are decreased in blood and/or bronchoalveolar lavage fluid.~~

~~68. A method of increasing interferon-α in connection with a disease, disorder, or trauma in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal, the method comprising administering a therapeutically effective amount of a composition comprising integrin α10-selected Mesenchymal Stem Cells (MSCs).~~

~~69.~~20. ~~A~~ Use of a composition comprising integrin alpha10-selected Mesenchymal Stem Cells (MSCs), for ~~use~~ the manufacture of a medicament ~~in a method of~~for

-preventing blood clotting,
-promoting hemodynamic stability,
-reducing the need for inotropic support,
-improving oxygenation capacity,
-preventing tissue damage, for example structural tissue damage,
-reverting tissue damage, for example structural tissue damage,
-reducing neutrophil counts,
-increasing lymphocyte counts,
-decreasing proinflammatory cytokines, and/or
-increasing interferon-α,

in a mammal in connection with a disease, disorder, or trauma of the respiratory system, and/or in connection with transplantation of an organ or tissue of the respiratory tract of a mammal.

~~70. The method according to claim 69, wherein the tissue damage is lung tissue damage.~~

~~71. The method according to any one of claims 69 to 70, wherein the tissue damage is damage of the interstitial tissue, damage of the alveolar septa, damage of the airways, damage of the vasculature, damage of muscle and/or damage of the nervous system.~~

~~72. The method according to claim 69, wherein the proinflammatory cytokines are selected from the group consisting of interleukin 12 (IL-12), IL-1β, IL-6 and IL-4, or any combination thereof.~~

~~73. The method according to any one of claims 69 to 72, wherein the proinflammatory cytokines are decreased in blood and/or bronchoalveolar lavage fluid.~~